IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TAKE2 TECHNOLOGIES LIMITED, and THE CHINESE UNIVERSITY OF HONG KONG,
 	
            Plaintiffs,
 	
    v.
 	
PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
 	
            Defendant.
	C.A. No. 22-cv-1595-MN

PACIFIC BIOSCIENCES' OPENING BRIEF IN SUPPORT OF MOTION TO DISMISS

Dated: February 14, 2023

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I. NATURE AND STAGE OF THE PROCEEDINGS

On December 14, 2022, Plaintiff Take2 Technologies Limited ("Take2") and Nominal Plaintiff The Chinese University of Hong Kong ("CUHK") (collectively "Plaintiffs") filed a complaint against Defendant Pacific Biosciences of California, Inc. ("PacBio"), alleging infringement of U.S. Patent No. 11,091,794 ("the '794 Patent"). PacBio now moves to dismiss the complaint for failure to state a claim.

II. SUMMARY OF THE ARGUMENT

The complaint here asserts one claim of one patent. D.I. 8, ¶ 36. This case is ripe for dismissal based on Section 101 on the pleadings because the invalidity of this patent is straightforward.

The '794 Patent claims a statistical model for calculating an allegedly better prediction as to whether a nucleic acid base is modified. A statistical model is ineligible subject matter because it is essentially math, even if it solves a problem of genetic prediction. *In Re Board Of Trustees Of Leland Stanford Junior*, 991 F.3d 1245, 1246-50 (Fed. Cir. 2021).

Insofar as Plaintiffs contend that the specific inputs used for the claimed statistical model are the supposed patentable innovation that saves the patent, they are wrong on the law. Selecting the particular inputs of a statistical model is merely selecting the terms of a mathematical formula and is not patentable subject matter. *See, e.g., Wisk Aero LLC v. Archer Aviation Inc*., No. 3:21-cv-02450-WHO, 2022 WL 1157489, at *3-8 (N.D. Cal. Apr. 19, 2022) (selecting the particular inputs for a statistical model is not patentable subject matter, even if novel).

The motion should be granted.

III.   STATEMENT OF FACTS

The '794 Patent describes the use of a statistical model to determine whether nucleotides (bases) are modified. Ex. 1, Abstract ("Machine learning models can be trained to detect the base modifications using these features.").

A statistical model is at the heart of the claimed inventions of the '794 Patent. The model uses the measured values of properties of a sample known to have a particular trait to correspond those values with the presence of the trait. Once the model is "trained," it can predict whether the particular trait is present simply by measuring the values of the associated properties and inputting them into the model.

The claims include four data manipulation steps that can be summarized as follows:

(1) **Receiving data** via an optical signal that measures four "properties" of each base in a nucleic acid strand, such as DNA, during sequencing.

(2) **Creating a data structure** from the received data of the sequenced nucleic acid strand that corresponds to the four properties.

(3) **Inputting the data structure into a model** that corresponds the values of the four properties of each base to whether a base is modified by using training samples in which it is known whether the base is modified.

(4) **Determining, using the model**, whether the modification is present in a nucleotide in the input data structure.

The claims specify that the four properties inputted into the model are: (1) the identity of each base such as whether it is a "T" base,[1] (2) its position in the nucleic acid strand, (3) the width

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[1] The conventional description of DNA is that there are four basic types of bases denominated "A," "C," "T" and "G." *Ass'n for Molecular Pathology v. Myriad*, 569 U.S. 576, 581 (2013). ("The possible nucleotides are adenine (A), thymine (T), cytosine (C), and guanine (G)").

of the pulse from the optical signal, and (4) the time duration between the pulse measuring the

base on the strand and the pulse measuring a neighboring base.

The complaint only alleges infringement of claim 1. D.I. 8, ¶ 36.

IV.   LEGAL STANDARD

A.   This One-Patent Case Is Ripe For Dismissal On A Motion To Dismiss

While some cases with numerous asserted claims or many patents may not be ripe for

resolution on a Section 101 motion by FRCP 12(b)(6), this is a single patent suit involving only

one pled claim. D.I. 8, ¶ 36. It is ripe for resolution now.

"Patent eligibility can be determined at the Rule 12(b)(6) stage when there are no factual

allegations that, taken as true, prevent resolving the eligibility question as a matter of law."

TrackTIME, LLC v. Amazon. com, Inc., No. 18-1518 (MN), 2019 U.S. Dist. LEXIS 102375, at *2

(D. Del. June 19, 2019) (quoting *Aatrix Software, Inc. v. Green Shades Software, Inc*., 882 F.3d

1121, 1125 (Fed. Cir. 2018)) (alterations omitted); *Sandbox Software, LLC v. 18Birdies, LLC*, No.

18-cv-1649 (MN), 2019 WL 2524780, at *1 (D. Del. June 19, 2019) (same). "[A] court need not

'accept as true allegations that contradict matters properly subject to judicial notice or by exhibit,'

such as the claims and the patent specification." *Id.* (quoting *Secured Mail Sols. LLC v. Universal*

Wilde, Inc., 873 F.3d 905, 913 (Fed. Cir. 2017)).

B.   Section 101 Is A Threshold Issue

Section 101 is a "threshold" issue. *Bilski v. Kappos*, 561 U.S. 593, 602 (2010). The *Alice*

two-step inquiry governs this motion. *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, 573 U.S. 208

(2014). "The court must first determine whether the patent's claims are drawn to a patent-ineligible

concept – *i.e.*, are the claims directed to a law of nature, natural phenomenon, or abstract idea?"

Realtime Data LLC v. Array Networks Inc., et al., 556 F.Supp.3d 424, 431 (D. Del. 2021). "If the

answer to this question is no, then the patent is not invalid for teaching ineligible subject matter."

Id. "If the answer to this question is yes, then the court must proceed to step two, where it considers 'the elements of each claim both individually and as an ordered combination to determine if there is an 'inventive concept – *i.e.*, an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Id.*

"It is well-settled that mere recitation of concrete, tangible components is insufficient to confer patent eligibility to an otherwise abstract idea. Rather, the components must involve more than performance of 'well-understood, routine, conventional activities' previously known to the industry.'" *In re TLI Commc'ns LLC Patent Litig.*, 823 F.3d 607, 613 (Fed. Cir. 2016).

V.   ARGUMENT

A.   The '794 Patent Is Invalid Because It Claims Ineligible Subject Matter

1.   *Alice* Step 1

The claims in the '794 Patent are directed to the abstract idea of using a statistical model to predict what modified bases are present in a nucleic acid strand such as DNA. The claims require four steps, which as explained above, center around the use of a model to predict whether a base is modified. *See* Statement Of Facts.

Plaintiffs' complaint specifies that the supposed invention is the ***statistical model***. For example, in their complaint CUHK and Take2 allege that "the Take2/CUHK Team ***invented a new neural-network-based model*** they coined the 'holistic kinetic' (HK) model."[2] D.I. 8, ¶ 13; *see also id.*, ¶ 22 ("PacBio did not stop working to commercialize the HK ***model*** without permission— even after having been notified of the '794 Patent."). The patent itself refers to a statistical model more than 30 times.

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[2] Emphasis supplied throughout.

Because the claims focus so heavily on a statistical model as the supposed invention, the claims are plainly directed to an abstract idea and *Alice* Step 1 is satisfied. Here, the statistical model is used as a tool; there is no improvement on computer technology itself. *Customedia Techs., LLC v. Dish Network Corp.*, 951 F.3d 1359, 1364 (Fed. Cir. 2020) ("[I]t is not enough, however, to merely improve a fundamental practice or abstract process by invoking a computer merely as a tool."). "In cases involving software innovations, the step-one inquiry often turns on whether the claims focus on specific asserted improvements in computer capabilities or instead on a process or system that qualifies as an abstract idea for which computers are invoked merely as a tool." *International Business Machines v. Zillow Group*, 50 F.4th 1371, 1377 (Fed. Cir. 2022).

This case is similar to *In Re Board Of Trustees Of Leland Stanford Junior*, 991 F.3d 1245 (Fed. Cir. 2021) – also a biotech case in which the claimed invention centered on improved statistical modelling. There, the claims described predicting haplotypes using an improved statistical model.[3]

The Federal Circuit concluded that the claimed inventions were ineligible for patenting because they involved an improved statistical model. *Id.* at 1246 ("the rejected claims are drawn to abstract mathematical calculations and *statistical modeling*, and similar subject matter that is not patent eligible."). The *Stanford* court explained that statistical modeling, even if better modeling, is not eligible for patenting because it is math:

> Specifically, the claims are directed to the use of mathematical calculations and *statistical modeling*. Courts have long held that mathematical algorithms for performing calculations, without more, are patent ineligible under § 101. *See, e.g.*, *Parker v. Flook*, 437 U.S. 584, 595, 98 S.Ct. 2522, 57 L.Ed.2d 451 (1978) ("[I]f a claim is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory." (internal citation omitted)); *Gottschalk v. Benson*, 409 U.S. 63, 71-

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[3] "Haplotype phasing is a process for determining the parent from whom alleles—i.e., versions of a gene—are inherited." *Id.* at 1247.

> 72, 93 S.Ct. 253, 34 L.Ed.2d 273 (1972) (finding claims patent ineligible because they "would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself"); *In re Schrader*, 22 F.3d 290, 294 (Fed. Cir. 1994) (a data gathering step of entering bids was "insufficient to impart patentability to a claim involving the solving of a mathematical algorithm").

Id. at 1250.

The Federal Circuit rejected Stanford's citation to other Federal Circuit cases finding software patents viable. It found that those cases "involve practical, technological improvements extending beyond improving the accuracy of a mathematically calculated statistical prediction." *Id.* at 1251. Here, the '794 Patent is directed to improving the accuracy of the statistical prediction that a nucleic acid base is modified and uses the computer as a tool.

Even if the inclusion of particular inputs used for the model were innovative that could not save the '794 Patent. In *Wisk Aero*, the district court applied *Stanford* to invalidate patents covering an improved statistical model for controlling the flight of an aircraft. *Wisk Aero LLC*, 2022 WL 1157489, at *4-6. The district court explained that "the method [of independent claim 1] 'receiv[es]' inputs and 'comput[es]' an 'optimal mix' of actuators and parameters." *Id.* at *4 (quoting '099 Patent, Cl. 1). The patentee contended that the innovation was the selection of novel inputs for the model to control the flight path. *Id.* ("To address this problem, the claims recite modeling a weighted set of costs [of errors], and they include within that set of costs a novel consideration of the cost.") (quoting Opposition to the Mot. 1).

The *Wisk* court rejected the argument because using novel parameters as inputs for a statistical model is simply adding a new mathematical step, which is itself patent ineligible because it is abstract. *Id.* at *5 ("That is precisely what makes them ineligible: including a new mathematical step in the computational technique."). The court explained why it is not patent eligible subject matter to add novel parameters for a statistical model:

> The advance of the '099 Patent over the prior art, it claims, is the technique of

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minimizing weighed costs. *See, e.g., id.* at 3:10-25*. **That, however, is just factoring in specific inputs into the equation in a specific way.*** Indeed, the specification explicitly contrasts this approach with previous mathematical techniques. *See id.* Performing this calculation is simply a "method[] which can be performed mentally, or which are the equivalent of human mental work," and is, therefore, an "unpatentable abstract idea[]." *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011).

Id. at *4.

Although Plaintiffs attempt to plead around the ineligibility of the '794 Patent in the complaint, they only do so with respect to Step 2. Step One is satisfied.

2. *Alice* Step 2

A patent claim directed to an abstract idea can be saved from ineligibility if it includes a patent eligible inventive advance. *Stanford,* 991 F.3d 1245, 1251 ("At step two, we inquire whether any limitations establish an inventive concept that transforms the abstract idea into patent eligible subject matter."). "Step two is like a lifeline: it can rescue and save a claim that has been deemed, at step one, directed to non-statutory subject matter." *Id.*

During prosecution of the '794 Patent, Plaintiffs argued that their claims were not invalid because the "input data structure is not well-understood, routine, or conventional at least because obtaining all the values for the listed properties is not well-understood, routine, or conventional, let alone combining into an input data structure and inputting into a model." Ex. 2 at 17.

Plaintiffs' position fails. The supposed unconventionality of the selection of the four properties to input into the claimed model is legally disqualified from constituting eligible subject matter. The abstract idea of adding new parameters to a statistical model cannot as a matter of law provide the "something more" for step 2. *BSG Tech LLC v. Buyseasons, Inc.*, 899 F. 3d 1281 (Fed. Cir. 2018) ("It has been clear since *Alice* that a claimed invention's use of the ineligible concept to which it is directed cannot supply the inventive concept that renders the invention 'significantly more' than that ineligible concept."). The selection of the parameters to use for a mathematical

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calculation is just as abstract as the model itself. To wit, a mathematical formula is not patentable merely because the parameters used in the formula are novel. In *Wisk*, the court explained that, under governing law, even the addition of innovative parameters to a statistical model is abstract math, as explained above. The *Wisk* court confirmed in its Step 2 analysis that this cannot constitute a patentable inventive concept because it too is, at bottom, construction of a mathematical calculation:

> Wisk's counterarguments illustrate that the patents are invalid, rather than pointing the other way. Wisk argues, on the '099 Patent, that "the inventive step is taking the . . . error[] between the requested force or moment and the calculated achievable force or moment and factoring that error into the analysis as a cost to be minimized." Oppo. 19. I agree. But that inventive step is nothing more than a mathematical step and "[t]he different use of a mathematical calculation, even one that yields different or better results, does not render patent eligible subject matter." *Stanford*, 991 F.3d at 1251.

Wisk Aero LLC, 2022 WL 1157489, at *7. Any attempt to rely on the supposed novelty of choosing the four claimed parameters for the statistical model fails because as a mathematical step it cannot constitute an inventive advance.

Insofar as Plaintiffs' vague Step 2 prosecution history argument suggests that actually "obtaining" the values of the four properties to use in the statistical model is somehow itself unconventional, that is a non-starter. Numerous references incorporated into the '794 Patent disclose the accessibility of the values for those four properties. *See, e.g.*, Ex. 3 at 2 ("This method takes advantage of kinetic data pertaining to the rate of incorporation of each dNTP in the form of two parameters—the pulse width (PW) and the interpulse duration (IPD)."); Ex. 4 at 2 (The change in IPD between a modified and control template varies in magnitude and position depending on the nature of the base modification and the local sequence context. We refer to these reproducible changes in IPD as the kinetic signature for that modification."); Ex. 5 at 2-3 ("Fluorescence pulses in SMRT sequencing are characterized not only by their emission spectra, but also by their duration

and by the interval between successive pulses. These metrics, defined here as pulse width (PW) and interpulse duration (IPD), add valuable information about DNA polymerase kinetics."), 3 ("we conclude that, in general, the kinetic signatures of methylation will be sequence context dependent"); Ex. 6 at 130 ("While there is a fair degree of stochastic variation in the IPD and PW values over different reads covering a common genomic region, reproducible variations in IPD and PW are induced as a result of modifications to the bases, as has been previously shown") (citing Ex. 5). The '794 Patent incorporates all of these publications by reference. Ex. 1 at 112:24-26.

Indeed, during prosecution the examiner even cited U.S. Patent No. 9,175,338 to Flusberg, which shows in the prior art the accessibility of the four parameters: (1) the identity of the base (A, C, G or T), (2) the location of the base, (3) the pulse width (PW) and (4) the interpulse duration:

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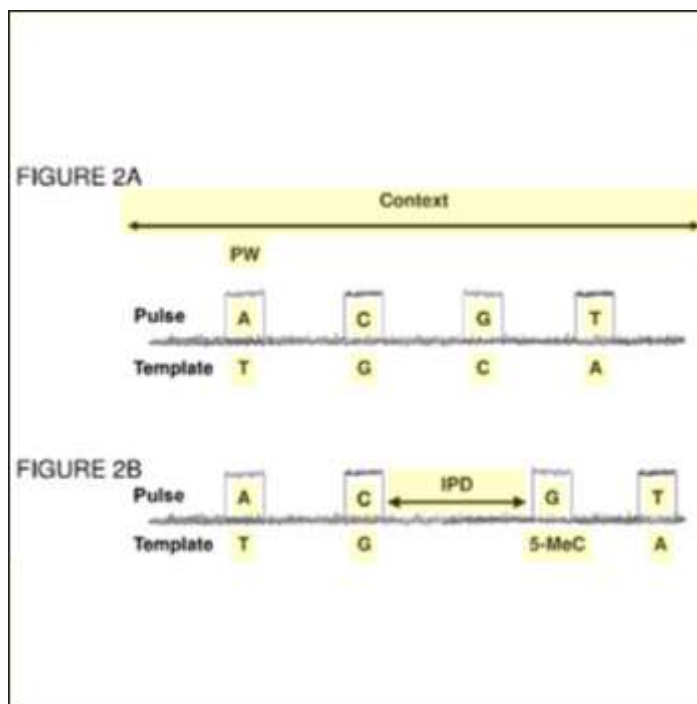
Ex. 7, Fig. 2 (annotated); Ex. 8 at 10-13.

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Thus, actually obtaining the values is not an inventive concept because these values were well known. And using these particular inputs for a statistical model is merely an additional mathematical step that is not patent eligible per *Stanford* and *Wisk,* as explained above.

That the Patent Office issued the '794 Patent does not change the analysis. The Patent Office applied agency guidelines that are not the law. *In re Rudy*, 956 F.3d 1379, 1383 (Fed. Cir. 2020) ("[W]e apply our law and the relevant Supreme Court precedent, not the Office Guidance, when analyzing subject matter eligibility. To the extent the Office Guidance contradicts or does not fully accord with our caselaw, it is our caselaw, and the Supreme Court precedent it is based upon, that must control."). The examiner did not explain how these claims could have satisfied the *Alice* analysis. And the '794 Patent issued before *Stanford* or *Wisk* were even decided.

The Plaintiffs' attempt to plead around *Alice* Step 2 is also futile. In paragraph 64, Plaintiffs merely assert that there is an inventive concept because the patented methods "improve the length and accuracy of 'detection of a modification' over prior art methods." D.I. 8, ¶ 64 (quoting Ex. 1 at 20:26-41). But a prediction based on a better statistical model does not make the model patentable merely because it is more accurate than the prior art. *Stanford,* 991 F.3d at 1252 ("That a specific or different combination of mathematical steps yields more accurate haplotype predictions than previously achievable under the prior art is not enough to transform the abstract idea in claim 1 into a patent eligible application.").

In paragraph 65, Plaintiffs allege that PacBio admits that the claimed method is unconventional and generates improved predictions, citing two publications. D.I. 8, ¶ 65. This is incorrect. The publications that Plaintiffs cite lack any connection to the '794 Patent at all. Moreover, a method of using a computer model is not transformed into patentable subject matter because it provides more accurate predictions even if Plaintiffs did discover novel parameters.

This is because the discovery of novel inputs to a statistical model is not patentable subject matter as explained above.

Even if Plaintiffs had asserted the dependent claims, that would not save their case. None of those claims add anything patentable to the statistical modelling method of claim 1. Nor would they be properly asserted – which is presumably why they are not included in the complaint. Those claims cannot save the case, even assuming they were asserted.

VI.   CONCLUSION

For the foregoing reasons, Plaintiffs' complaint should be dismissed.

February 14, 2023

Respectfully submitted,

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